

(様式1)

公益社団法人日本栄養・食糧学会 研究業績

<学 会 賞>

1. 候補者

研究題目:(和)	寝たきりや無重力による筋萎縮のメカニズム解明とその栄養学的治療法の開発		
(英)	Molecular mechanism and nutritional approach for unloading-mediated muscle atrophy		
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所属機関:(和)	徳島大学 大学院医歯薬学研究部 生体栄養学分野		
(英)	Department of Nutritional Physiology, Institute of Medical Nutrition, Tokushima University Graduate School		
学 位:	博士(医学)	最終学歴:	平成3年3月 徳島大学大学院医学研究科博士課程 修了
専門分野	①栄養生理学、③分子栄養学、⑱その他(宇宙生物学)		
履 歴	平成 3年 4月 徳島大学医学部附属病院検査部基礎系医員 4年 5月 ドイツ国デュッセルドルフ大学医学部第一生理化学研究室 研究員 6年 2月 徳島大学助手医学部栄養学科栄養生理学講座 15年 12月 徳島大学助教授医学部栄養学科栄養生理学講座 19年 9月 徳島大学大学院教授ヘルスバイオサイエンス研究部 生体栄養学分野(平成27年度より医歯薬学研究部に改組) 23年 4月 宇宙航空研究開発機構 有人宇宙技術部 宇宙医学生物学研究室 主任研究員(平成26年3月まで) 27年 4月 徳島大学医学部医科栄養学科長併任		
会員番号:		入会年度:	平成7年度

2. 研究業績要旨(1,000字以内)

無重力や寝たきりなど Unloading 環境は、生体にさまざまな影響をあたえる。なかでも、骨格筋の萎縮は著しく、運動器に急激な老化が進行したような状態を示す。そこで、私は宇宙フライトや尾部懸垂による骨格筋の萎縮のメカニズムの解明が、加齢などによる運動機能の低下の原因究明にもつながると考えた。Unloading 環境では蛋白質のユビキチン化が促進されるので、Unloading 環境に暴露したラットの腓腹筋の遺伝子を網羅的に解析し、そのユビキチン化の原因遺伝子を探索した。その結果、増殖因子のレセプターやその関連蛋白を特異的にユビキチン化させるユビキチンリガーゼ Cbl-b (Casitus B-ligeage lymphoma-b)の発現が宇宙フライトにより増大していることを発見した。Cbl-b は、インスリン受容体基質蛋白質 (IRS-1)をユビキチン化し分解へと導くユビキチンリガーゼとして働き、骨格筋におけるインスリン様増殖因子のシグナル伝達を負に調整していた。また、Cbl-b ノックアウトマウスでは Unloading による筋萎縮がほとんどおこらなかった。これらの所見より、Cbl-b が筋細胞の増殖因子受容体シグナル系を負に調節し、筋萎縮を引き起こす重要な筋萎縮関連遺伝子の一つであることがわかった。この分子をターゲットにして、そのユビキチン化を阻害できる栄養素材も発見した(2件の特許取得)。それは、Cbl-b と IRS-1 の結合に対する阻害活性を有する DG(p)YMP ペプチド (Cblin ペプチドと名付けた) とその類似配列をもつ大豆グリシニンタンパク質である。これらは *in vitro* や *in vivo* 実験において Cbl-b による IRS-1 のユビキチン化を抑制し筋量を増大させた。また、大豆タンパク質添加食は寝たきり患者の筋力減少の抑制にも有効であった。以上の知見から、リハビリテーション以外に治療法のない Unloading による筋萎縮に対する新しい栄養学的治療法の概念も提唱している。さらに、この Cbl-b の発現調節機構を解明することにより、骨格筋が Unloading ストレスをどのように感知しているかについても研究を進めている。その結果、筋細胞のミトコンドリアから産生される酸化ストレスが Unloading ストレスの感知に重要な働きをしていることも明らかになりつつある。

3. 報文等リスト

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(3) 過去 5 年間の本学会での活動状況

【大会・支部会での座長・シンポジスト】

平成 22 年度

- ・第 43 回中国・四国支部会において特別講演
演題「無重力や寝たきりによる筋萎縮の分子メカニズム」

平成 24 年度

- ・第 66 回大会 シンポジウム「運動トレーニングと安静のアミノ酸栄養」座長及びシンポジスト
演題「廃用性筋萎縮の分子メカニズムと栄養学的治療」
一般演題「栄養生理:タンパク質・アミノ酸代謝(4)」座長
- ・第 45 回中国・四国支部会 座長

平成 25 年度

- ・第 67 回大会 シンポジウム「ペプチドが拓く健康科学の新しい世界」シンポジスト
演題「廃用性筋萎縮改善ペプチド」

平成 26 年度

- ・第 68 回大会一般演題「病態・臨床栄養：脂質異常症 2」座長

平成 15 年から現在まで 日本栄養・食糧学会 参与、中四国支部会 評議員

平成 21-22 年度 日本栄養・食糧学会 広報委員

(4) 特記事項

平成 12 年度 第 54 回日本栄養・食糧学会大会 奨励賞受賞

「サイトカイン受容体欠損マウスを用いた小腸粘膜免疫能に対するビタミン A の賦活効果の解析」

JAXA と共同で「無重力による筋萎縮のメカニズムとそれに効果のある機能性宇宙食の開発」を目指して 4 回の宇宙実験を施行した。